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# Physics of binding between cell-adhesion molecules (CAMs) in biosamples

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**Abstract** : The binding mechanisms in biological systems which are very useful to explain the pattern formation are discussed on the physics like model of interaction due to CAMs. The morphogenesis of animals is discussed from the analogy of one dimensional systems with interactions equivalent to cell-cell and cell-background interactions in biosamples. Some very interesting comments can be made regarding the color morphogenesis of some animals by drawing the analogy from one dimensional Ising model.

**Keywords** : Morphogenesis, Ising model, pattern formation.

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## 1. Introduction

The structural and dynamical constraints that the molecular and cellular structure of the living organisms impose on the process of morphogenesis and evolution are of great importance as these constrains might drastically restrict the choices allowed to adaptive mechanisms in order to solve problems of environments. The animals and plants are built of discrete units, the cells, at the organization level. For an organ, the number of cell type is small but there is a unique basic cell which can be in a finite small number of states [1]. The cells interact with other neighboring cells through short range interactions due to forces between macromolecules in their surfaces.

By convention, we call the binding of similar cells as homotypic and the binding of similar molecules as homophilic. It is possible to have a homophilic mechanism to get heterotypic binding (between different kind of cells). The interaction might take place among equivalent cells (different states of basic cells) or between those cells which have cellular or acellular background.

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It might happen that the organization pattern favoured by the equivalent cell interaction was different from the pattern favored by the cell-background interaction. A conflicting competition between both these interactions will be present and the organization pattern which resolves this conflict will depend on the relative importance of each of the two interactions.

We discuss in the present case, the binding mechanism in biological systems by two scenario which are very useful in pattern formation and are assumed to be based on the principle of models of physics *e.g.* one and two dimensional discrete systems (in a lattice) at zero temperature and with conflicting interactions. We consider the situations in which (i) the time evolution of the cells is slow enough so that the cells might accommodate reaching a global minimal energy configuration consistent with the conflicting constraints. (ii) The freezing of pattern takes place fast enough and there will be no time for minimal energy accommodation. The pattern of the successive rows or sheets will depend on the interaction with the preceding, already frozen, row or sheet of cells.

In this work, we will concentrate on the former case where the time evolution allows a global minimal energy accommodation and assume the short range interactions between the neighboring cells and use the idea to model the morphogenesis of color patterns of some animals.

## 2. Cell-Cell interactions

The interactions among cells in animals and plants can be associated with two basic mechanisms : (i) short range interactions due to macro molecules which are present at the cell surface. These molecules may interact with similar molecules at the surface of neighboring cells. (ii) The diffusion of chemicals, which originate at the cells can be the origin of attractive or repulsive effective long range interaction. These interactions depend on the activation rate, inhibition rate and diffusion coefficients.

The short-range interactions due to cell adhesion molecules (CAMs) will be more important for the nearest neighboring cells. Therefore, if the interaction due to CAMs is modeled in 'Physics-like' language, one would expect the dominance of nearest neighbor interactions between the elements and the existence of these short range interactions will impose restrictions on the dynamics of morphogenesis. We intend to model the interactions due to CAMs by discrete one or two dimensional systems with conflicting interactions. For example, these interactions can be modeled in polymers and surface absorption. Our calculations are based on Bak and Bruinsma model with one dimensional lattice site.

## 3. Discrete systems with conflicting interactions

Many physical systems can be modeled by discrete one or two dimensional systems with conflicting interactions. We can classify the discrete systems with $k$ number (say) of states allowed to the elements. In this work, we will assume that the number of allowed states is two. The model [2] assumed in the present case is one-dimensional Ising model and the complete Devil's stair case. The Hamiltonian of the system may be written as

$$H = -\sum_i H'\sigma_i + \sum_{i \neq j} J(|i-j|)(1+\sigma_i)(1+\sigma_j). \qquad (1)$$

The indices $i$ and $j$ label the sites of the one-dimensional lattice and the assumed spin variable $\sigma$ can take two values : $\sigma = \pm 1$. The function $J(|i-j|)$ is non-negative and depends on the distance $(|i-j|)$ between sites and is decreasing and convex. $H'$ represents a common external field and is always positive. Now due to the presence of the term $(1+\sigma_i)(1+\sigma_j)$, the interaction will be non-zero if $\sigma_i = \sigma_j = 1$ and zero otherwise. The Hamiltonian (eq. (1)) can be used to model one-dimensional ferromagnetic systems, lattice gas and alloys. Bak and Bruinsma [2] have analysed the possible configurations which minimizes the energy of eq. (1) as shown in Figure 1. If there was no external field *i.e.*

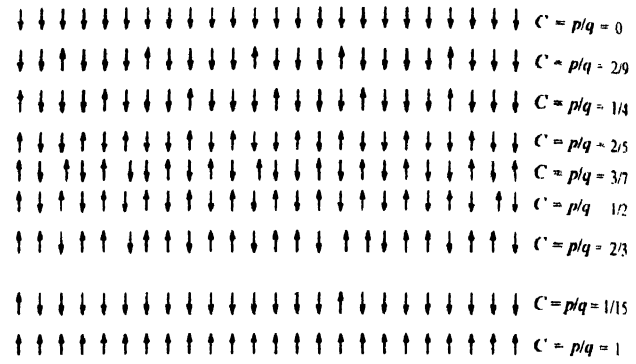


**Figure 1.** Stable spin configurations given by the ground states of one dimensional Ising model with convex long range interaction, $C$ is the ratio of particles in the up spin state to the total number of particles

$H' = 0$, the energy will be minimal if for all values of $i$ and $j$ (all sites) $\sigma_i = \sigma_j = -1$.

If $J(|i-j|) = 0$, the first term of eq. (1) implies that the energy will be minimal if $\sigma_i = 1$ for all values of $i$ (all sites) Now if both $H'$ and $J(|i-j|)$ are non-zero terms, the minimal energy configuration will depend on the relative strength of $H'$ and $J(|i-j|)$. Then there will be a conflict between the actions of both terms of eq. (1).

For a given external field, the problem of minimizing eq. (1) is equivalent to the problem of arranging a number of charged particles on $N$ sites so as to minimize the Coulomb energy and has been solved by Hubbard [3].

In order to find minimal energy configuration, Bak and Bruinsma [2] considered two steps

(i) For a given values of $H'$ and $J$, the conflict fixes the values of the ratio $C = \dfrac{n_{+1}}{(n_{+1}+n_{-1})}$, where $n_{\pm 1}$ is the number of sites with $\sigma = \pm 1$.

(ii) For given value of $C$ (*i.e.* for a given number of sites with $\sigma = 1$), it has been proved that the non-negative, decreasing and convex character of $J(|i-j|)$ implies that the energy will be minimal if the sites with $\sigma = 1$ are 'as separated as possible'.

An algorithm to compute this configuration has been found for rational values of the ratio $C$. Let, $X_i^0$ denotes the position of the $i$-th up spin, and let $X_i^p$ is the distance to the $p$-th nearest up sipn, $X_i^p = X_{i+p}^0 - X_i^0$. If the fraction of up spin is $q = m/n$, it can be shown that the energy is minimized if for all sites, then

$$X_i^p = r_p \text{ or } r_p + 1,$$

where $r_p < np/m < r_p + 1$. For $p/q = pn/m$ integer, $X_i^p = r_p = np/m$. Considering these, we may discuss some configurations *e.g.* $C \leq 1/2$ as follows. If $C$ is 1, 1/2,

1/3, ..., 1/*n*, ... (*n* is an integer), it is easy to see that for fields *e.g.* Coulomb potential, the lowest energy configuration is that in which all the electrons are equally spaced *a* distance of *n* neighbors which is the one dimensional analogue of classical Wigner lattice.

Suppose now that *C* does not take one of the specific values 1/*n*. The next simplest case is that in which *C* has the form 2/5, 2/7, 2/9, ..., 2/(2*n*+1), ... (*n* is an integer), in which the electrons are arranged themselves alternately intervals of *n* and *n* + 1. Infact, for any density *C* in between, are always equal to either *n* or *n* + 1. For *C* of special form,

$$C = \frac{m+1}{mn+n+1} = \left[n + \frac{1}{m+1}\right]^{-1},$$

where *m* and *n* are integers. The arrangement consists of periodically repeating configuration with period *nm* + *n* + 1, the (*m* + 1) electrons in each period arranging themselves with *m* intervals *n* and interval (*n* + 1).

For densities of the form,

$$C = \frac{(m+1)}{(mn+n-1)} = \left[n - \frac{1}{m+1}\right]^{-1},$$

where *n*, *m* are integers. The period is *mn* + *n* − 1 of the (*m* + 1) electrons in each period are arranged with *m* intervals of *n* and one interval of (*n* − 1).

For densities of particular form,

$$\frac{1}{C} = n + \frac{(p+1)}{[p(m+1)+m+2]},$$

where *n*, *m*, *p* are integers, which are periodically repeating units.

Also this can be done by graphical configurations as shown in Figure 2.

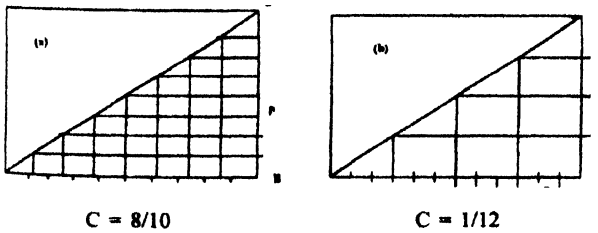


**Figure 2.** Construction to distribute *p* elements in *q* sites of a one dimensional lattice : (a) *C* = 4/5, (b) *C* = 1/3. The dots indicate the position of the *p* elements.

(a) In the absence of the constraints due to the presence of the lattice if the ratio *C* is equal to *p*/*q* (*p* and *q* are integers) the energy will be minimal if *p* elements with $\sigma = 1$ are equal spaced in length *q*. However, for this equal spacing solution, the *p* elements would not be integral in the lattice points.

(b) Due to discrete character of the lattices, we displace each of the *p* elements to the nearest site of the lattice. In order to divide, a length *q* in *p* equal segments we may do the following :

(i) a horizontal line segment (*A*, *B*) of *q* units is drawn. (ii) From the right extreme of the segment (*B*), a vertical segment with a length of *p* equal spaced units (*B*, *C*) is drawn and a straight line from the left point of the horizontal segment (*A*) to the upper point of the vertical one (*C*) is also drawn. (iii) From the equal spaced *q* points of the vertical segment, horizontal lines to the diagonal line (*A*, *C*) are drawn. (iv) From these intersection points, we draw vertical lines. These lines will divide the horizontal line (*A*, *B*) in *p* segments of equal length. The points which separate the *p* segments do not coincide, in general, with the lattice sites. (v) Each *p* point is moved to the nearest point of the lattice. If the point is at equal distance from two lattice sites, move it to the right side one. This construction will solve the problem.

## 4. Importance of $J(|i-j|)$ and the allowed values of *C*

To make the distribution of *p* sites as equal spaced as possible in *q* equal spaced places, the allowed values of the ratio *C* = *p*/*q* will depend on $J(|i-j|)$ and on $H'$ for a given values of $J(|i-j|)$ [4]. The importance of $J(|i-j|)$ will depend on the strength of the interaction for a given *n*-th neighbor and on the number of *n*-th neighbors. The total energy will be the sum of repulsive energy, which is positive and attractive negative energy. The negative energy arises due to the interaction with the external field. The repulsive positive energy will be a linear combination of the number of *n*-th neighbors and for the decreasing convex potential.

In order to model biological phenomena, the short-range character of the cell-cell direct interaction (first or at the most second or third neighbors) will imply simple ratios *p*/*q* the corresponding structure.

Cocho *et al* have calculated the minimal energy (patterns of one and two dimensional discrete systems with conflicting interactions) configuration for *p* elements in *q* sites of a square or triangular lattice for the Hamiltonian of equation and took $(|i-j|)$ as the distance between two points of the two dimensional lattice [5]. Then the configuration becomes as shown in Figure 3.

## 5. Application of the model to morphogenesis of color pattern

These structures may be compared with the morphogenesis of color patterns of many animals *e.g.* snakes such as the Krait and Coral show alternative dark and light segments of more or less equal size.

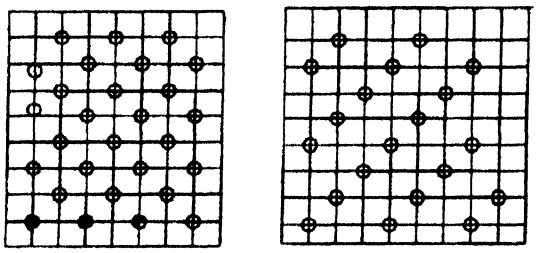

**Figure 3.** The equilibrium position of particles in a two-dimensional lattice for $C$ = 1/2 and 1/3 for square lattice.

The Hamiltonian of eq. (1) may be rewritten as :

$$H = -\sum_i H'\sigma_i + \sum_{i\neq j} J(|i-j|) \times (1+\sigma_i+\sigma_j+\sigma_i\sigma_j) \quad (2)$$

or $$H = K - h\sum \sigma_i + \sum_{i\neq j} J(|i-j|)\sigma_i\sigma_j, \quad (3)$$

where $$K = \sum_{i\neq j} J(|i-j|); \quad h = H' - 2\sum_j J(|i-j|). \quad (4)$$

This Hamiltonian (3) can be used to model the cell-cell and cell-background interaction. If $\sigma_i = +1$ corresponds to cells of type $A$ and $\sigma_i = -1$ to cells of type $B$, the last term of eq. (3) implies a larger value of energy (repulsion) if $i = j$ ($A$-$A$ or $B$-$B$) and a smaller value if $i \neq J$($A$-$B$). By adding a constant negative term, the repulsion will become no interaction (for $A$-$A$ and $B$-$B$) and the attraction for $A$-$B$ will increase. Therefore, we can model the heterotypic interaction. The term $-h'\Sigma_i\sigma_i$ would model the interaction with a cellular or acellular background.

Now these results are applied in order to model the morphogenesis of color patterns of some animals such as snakes, tail of lizards, felines and others of one dimensional domains.

In coral snakes, three color patterns (red, black and yellow or white) are seen to alternate in a periodic way. It is also seen in some of the Coral snakes that the tail and/ or the head show a two color pattern different from the body pattern. In order to model the morphogenesis of these color patterns, clonal hypothesis is used as follows : in an early stage, a small number of precursor cells of two or more types would accommodate or differentiate minimizing the energy of the cell-cell and cell-background interactions. This pre-pattern would freeze and each of the cell would divide, being the origin of a spot or region.

We will assume that in an early stage, a small number of precursor cells accommodate minimizing an energy function. If only first or at most second and third neighbor interactions are taken with a cellular or acellular background interaction, then in the first step a mechanism discriminates between dark (black) and light (red or yellow) precursors and a second mechanism would discriminate between red and yellow. It is well known that various pigment cells are derived from a stem cell that consists a primordial organelle of endoplasmic reticular origin [6]. This primordial cell would differentiate into any of the known pigmentary organelles. The primordial organelles would differentiate first into melanosome, reflecting platelet or pterinosome. It then differentiate into red or yellow chromosomes. To take into account of these facts, we now propose a model in terms of Hamiltonian and consider the formal dynamics, as follows :

The total energy,

$$E = E_1 + E_2, \quad (5)$$

where $$E_1 = -\sum h_1\delta_{\sigma i,B} + \sum J_1(|i-j|)\delta_{\sigma i,B}\delta_{\sigma j,B} \quad (6)$$

and $$E_2 = -\sum h_2\delta_{\sigma i,Y} + \sum J(|i-j|)\delta_{\sigma i,Y}\delta_{\sigma j,Y}. \quad (7)$$

Here, we have labelled by $B$ the black rings and $Y$ the yellow rings and $R$ the red rings. Also the $\delta_i$'s are the Kronecker delta functions with $\delta_i = B$, $Y$ or $R$.

Eq. (3) has solutions of alternating domains of the type shown in Figure 1 with up spin replaced by black and down spin replaced by yellow or red.

The solution of eq. (5) would break the yellow-red degeneracy and would produce structures with up replaced by yellow and down by red and finally, we get the structure as Figure 3. Here, we have taken $C_1 = p_1/q_1$ and $C_2 = p_2/q_2$ and associated to the action of $E_1$ and $E_2$ respectively.

If we redraw Figure 3 with the spots enlarged until they coalesce and without drawing the lattice we obtain the pattern similar to the coats of large cheetah.

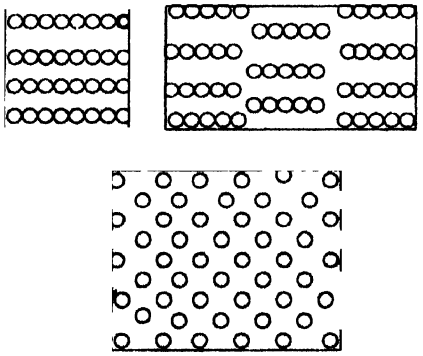

**Figure 4.** Coats of cheetah obtained from enlargement of dots in Figure 3.

## 6. Discussion

In this work, we reviewed some earlier works on the binding of biomolecules and discussed the point of view of the

models of physics applied to obtain the color patterns of biomolecules with some general features of short range cell-cell interactions. In fact, the color patterns have to be discussed from the numerical simulations of the proposed equations for suitable values of $J$. This we propose to do in our future work. However, the present model of minimization of the interaction energy has been discussed neglecting the chaotic motion of cells. The chaotic motion may be modeled and parameterized by means of temperature. Within the framework of a rather simple microscopical physical like modeling, the main features of colour patterns may be qualitatively discussed but the actual three dimensional pattern seems to be highly complex.

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